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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/241,595	02/02/1999	JORG REIMANN	9325-0008.30	8928

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EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/06/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/241,595	Reimann et al.
Examiner	**Art Unit**
Anne Marie Wehbé	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 27, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3-11, and 13-31* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3-11, and 13-31* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response and the declaration under 37 CFR 1.132 received on 12/2/02 have been entered. Applicant's explanation for why the declaration was submitted post-filing has been accepted. Claims 1, 3-11, and 13-31 are pending in the instant application. Please note that the finality of the previous office action has been **withdrawn** in view of new grounds of rejection presented below. An action on the merits follows.

The text of those sections of Title 35, US code, not included in this office action can be found in the previous action, paper no. 6.

Claim Rejections - 35 USC § 112

The rejection of pending claims 1, 3-11, and 13-31 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained in part. Applicant's arguments, the declaration by Dr. Reimann, and the exhibits have been fully considered but have not been considered persuasive in overcoming the following instant grounds of rejection for reasons of record as discussed in detail below.

The applicant's arguments, declaratory evidence, and exhibits have overcome the rejections of the claims based on the identity of the molecules to be entrapped within or exposed

on the surface of the claimed HBsAg particles, and the use of the those particles to stimulate or enhance CTL responses. In regards to the generation of CTL responses against HIV or HBV epitopes, the Office acknowledges that while the specification does not enable the treatment or prevention of diseases such as HIV, the generation of CTL responses against HIV epitopes is useful in maintaining the health of infected individuals.

A single issue remains in this scope of enablement rejection. The prior office actions have stated that the ability to generate CTL *in vivo* is significantly affected by the antigen and route of administration. Specifically, the previous office actions stated that genetics, dose or concentration of antigen, and route of antigen administration contribute to the unpredictability of generating CTL, helper T cell, and/or B cell responses in vivo (Abbas et al. and Golding et al). In response, the applicants argue that the skill level of those in the art of immunization is sufficiently high to determine what route of administration would be suitable for use in the instant invention. The applicant also states that the applicants are willing to amend the claims to incorporate the language "by an effective route". In response, the previous office actions have pointed out that while the specification and declaratory evidence have provided data demonstrating the induction of CTL responses to HBsAg particles comprising various cytokines, ODNs, and/or peptide antigens, none of these experiments disclose or provide guidance as to the route of administration. As such the specification fails to provide sufficient guidance to overcome the unpredictability associated with various routes of delivery of antigen and the generation of immune responses. Regarding applicant's willingness to include the language, "by and effective route", amendment of

the claims to include this language would be acceptable provided that the applicant can point to support in the specification for this language.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Please note that the following rejection was withdrawn in error in the previous office action, paper no. Therefore, prosecution in this case has been reopened and claims 1, 5-6, 11, 17-18, 25-27, and 29-30 have been re-rejected under 35 U.S.C. 102(b) over Neurath et al.

Claims 1, 5-6, 11, 17-18, 25-27, and 29-30 are newly rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,039,522 (8/13/91), hereafter referred to as Neurath. The applicant claims a composition comprising a biologically active molecule or antigenic molecule exposed or present at the surface of an HBsAg particle, wherein the molecule is not covalently attached to said HBsAg particle, methods of incorporating a biologically active molecule into HBsAg particles by incubating the biologically active molecule with HBsAg in aqueous media,

and methods of stimulating an immune response to an antigenic molecule or HBsAg by administering to a subject a composition comprising an antigenic molecule or immunostimulatory molecule exposed or present at the surface of an HBsAg particle. The applicant further claims said compositions and methods wherein the biologically active molecule is an antigen or immunostimulatory molecule, and wherein the composition further comprises a glycolipid incorporated into the exterior of the HBsAg particle .

Neurath teaches that it is possible to add any peptide with a hydrophobic tail to HBsAg particles to produce an immunogen useful for generating immune responses against viral proteins or peptides (Neurath et al., column 3, lines 39-51, columns 11-12, claims 1-17). Neurath further teaches that the peptide can be a naturally occurring or synthetic peptide derived from HIV or hepatitis B (Neurath, column 3, lines 46-62). Neurath also teaches the preparation of HBsAg particles which contain myristolated hepatitis B preS antigen by incubating myristolated preS protein with HBsAg in an aqueous media (Neurath, column 10, lines 13-48). Please note that while the peptide is covalently bonded to the myristal andehyde, Neurath et al. clearly indicates that the absorption of myristilated peptide to HBsAg particle is a **non-covalent** interaction (Neurath et al., column 11, lines 28-34). Furthermore, the absorption of the myristilated peptide into the HBsAg particle results in the presence of the peptide on the surface of the HBsAg particle as evidenced by the recognition of the complexed HBsAg with antibodies against the myristilated peptide. In addition, Neurath teaches the immunization of rabbits with the preS containing HBsAg particles resulting in the generation of anti-HBV antibodies (Neurath, column

11, lines 9-51). It is also noted that antigens are inherently considered immunostimulatory molecules as their expression results in the generation of immune responses. Thus, by teaching all the limitations of the claims as written, Neurath anticipates the instant invention.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER